

Session: MR Physics & Techniques for Clinicians

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Contrast Agents in MRI

The use of contrast agents in MRI started in 1983 with its first application in a patient scan. In 1988 the first contrast agent, Magnevist®, was approved for the clinical use. Numerous contrast agents were introduced to the market in the 90ies, most of them based on Gadolinium (Gd). Since Gd itself is biologically toxic, it is surrounded (or chelated) with ligands such as Gadopentetat-Dimeglumine (DTPA) for instance. Different Gd-based contrast agents are characterized by different Gadolinium (Gd) chelate structures. At present, most MRI examinations are performed using paramagnetic Gadolinium-based contrast agents.

Contrast agents can be divided into two subgroups: the positive agents appearing predominantly bright on MR images and the negative agents appearing dark on MR images. Gd-based agents belong to the positive agents causing both T1 and T2 relaxation time shortening. This results in high intensity on T1-weighted images. Shortening of T2 relaxation times causes a decreased signal but considering typical concentrations of contrast agents and typical echo times TE, the T1 shortening dominates the signal intensity. Negative contrast agents are small particulate aggregates often termed superparamagnetic iron oxide (SPIO, or ultrasmall SPIOs) consisting of a crystalline iron oxide core and a shell. These agents produce predominantly local field inhomogeneities resulting in very high T2 relaxivities.

The T1 shortening of Gadolinium-based contrast agents is used to increase the flip angle if data acquisition is based on a gradient echo sequence. Therefore, tissue (or blood) with a strongly decreased T1 time containing contrast agent provides a much higher signal intensity. An optimal flip angle (Ernst-angle) yielding the highest signal intensity can be calculated for gradient echo sequences (in the so-called steady state) based on TR and T1. Due to the higher flip angle, background tissues, i.e. tissues without an uptake of contrast agent, appear with relatively low signal intensity.

All extra-cellular contrast agents rapidly pass over from the intravascular compartment into the interstitial space. More than 80% typically leave the intravascular space within the first five minutes after the administration of the contrast agent. Therefore, a certain but relatively short acquisition window is given, with a length depending on the application. For instance, in contrast-enhanced angiography imaging must be conducted at the first arrival of the contrast agent bolus in the vessel of interest, i.e. within a few seconds after injection.

One class of contrast agents overcomes this constraint, the so-called blood pool contrast agents. Due to its bigger size – this is typically realized by a binding of a rather small agent itself with macromolecules, namely proteins – the contrast agent cannot leave the intravascular compartment, therefore extending the imaging window to hours. Due to their bigger size blood pool agents are characterized by a higher relaxivity thus providing higher signal intensity compared to extra-cellular contrast agents. Extra-cellular contrast agents exhibit only minor differences of relaxivities depending on the magnetic field strength. On the other hand, relaxivity alterations were larger (decreasing with higher field strengths) for contrast agents with protein binding, most pronounced in blood pool agents.

Contrast agents are applied for a variety of clinical questions, from angiography and tumor characterization over myocardial, cerebral or tumor perfusion to the representation of inflammation or myocardial necrosis. For all types of examinations the effect of T1 shortening is used providing high signal intensity in T1 weighted sequences except for cerebral perfusion. Here, a negative contrast is produced when the contrast agent appears in the brain vessels due to the use of a T2* weighted Echo Planar imaging (EPI) sequence.

In general contrast agents were considered as safe and well-tolerated, when in 2006, the disease nephrogenic systemic fibrosis (NSF) was linked to the administration of MRI contrast agents based on Gd in patients with renal insufficiency. Pathogenesis and etiology of NSF are still not fully understood. The apprehension about NSF has led to greater attention with respect to the dose of Gd applied for an MRI procedure since the risk for NSF increases with higher doses. The FDA approved dose is up to 0.3 mmol/kg body weight. However, it has been shown that for non-ionic linear chelates – revealing the most cases of NSF – that there is a negligible risk at 0.1 mmol/kg.

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